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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/777,484	02/05/2001	John H. Griffin	SCRIP1200-1	8867

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	PAPER NUMBER
1647	9

DATE MAILED: 10/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/777,484	GRIFFIN ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *17-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3, 6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the species of "stroke", "NMDA receptor antagonist", "anticoagulant agent", "streptokinase", and "any inhibitor of platelet glycoprotein IIb-IIIa" in Paper No. 8 (01 July 2002) is acknowledged. The traversal is on the ground(s) that the claimed subject matter in each group (the disease group, the neuroprotective group, the additional agent group, the thrombolytic group, the anti-platelet group) is related by a common operation, function, and effect, as cited in MPEP § 806.04(e). Applicant also submits that the search of all diseases, neuroprotective agents, additional agents, thrombolytic agents, and anti-platelet agents would not place an undue burden on the Examiner. This is not found persuasive because the claimed subject matter in each species group are not related by a common operation, function, or effect. For example, the disease group lists such disorders as stroke, epilepsy, mental retardation, and aging, all of which have different biological causes and effects. Additionally, each disease and agent listed in the species requirement of 22 May 2002 (Paper No. 7) is unique, requiring a unique search of the prior art. Searching all of the species in a single patent application would provide an undue search burden on the examiner because of the non-coextensive nature of these searches. Furthermore, Applicant asserts that the Examiner's identification of the generic claims of the invention is unclear and requests clarification of the identification of the generic claims of the invention. Regarding the disease group, claims 1-2, 5-10, 16-21 are generic. Regarding the neuroprotective agent group, claims 1-6 are generic. Regarding the additional agent group, claims 1-15 and 19-21 are generic. Regarding the

thrombolytic agent group, claims 1-16 and 18-21 are generic. Regarding the anti-platelet group, claims 1-17 and 19-21 are generic.

Claims 17-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8 (01 July 2002).

Claims 1-16 and 19-21 are under consideration in the instant application, as they read upon the elected species of "stroke", "NMDA receptor antagonist", and "anticoagulant".

Specification

1. The disclosure is objected to because of the following informalities:

2. The Brief Description of Drawings for Figures 6A-6E at pg 8 of the specification refers to Figure 7A instead of Figure 6A (see line 1).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-16 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of decreasing brain infarction volume and edema volume in a subject suffering from a stroke comprising administering to the subject an effective amount of activated protein C (APC) to thereby decrease brain infarction volume and edema volume in the subject, does not reasonably provide enablement for a method of protecting neuronal cells from cell death in a subject having or at risk of having a neuropathological

disorder comprising administering to the subject, a neuroprotective amount of activated protein C (APC). The specification is not enabling for a method of reducing inflammation in a subject having or at risk of having a neuropathological disorder by administering APC. The specification is also not enabling for a method of reducing inflammation in a subject having or at risk of having inflammatory vascular disease comprising administering APC. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Furthermore, the dependent claims recite that APC is administered intravenously during the stroke or up to 6 hours before or after the stroke. The claims recite that the method further comprises administering one or more anti-thrombotic factors, APC-cofactors, one or more additional neuroprotective agents (such as a N-methyl-D-aspartate receptor (NMDA) antagonist), one or more anti-coagulants, and one or more anti-inflammatory agents. The claims also recite that the APC cofactor is Protein S.

The specification of the instant application teaches that "mice treated with APC had a significant reduction in the volume of brain injury compared to control mice (Figure 2)" (pg 31, lines 17-18). The specification discloses that the total volume of injury of gray matter, i.e., brain infarction volume, is significantly decreased by 59% in the APC-treated group compared to control. The specification also discloses that the edema volume in the lesioned ischemic hemisphere is reduced by APC treatment by 50% (see pg 31, lines 18-24; Figure 2A-2B). Additionally, the specification discloses that the administration of APC post occlusion results in a reduction of infarction volume by 69% and edema volume by 61% (pg 33, lines 19-25; Figure 6A-6B). The specification teaches that co-injection of Protein S with a low dose of APC

produces a synergistic effect, significantly reducing brain infarction and edema by 71% and 51%, respectively (pg 35, lines 8-15; Figure 8A-8B). However, the specification of the instant application does not teach any methods or working examples to indicate that the administration of APC to a subject "protects" neuronal cells from cell death. The term "protect" in claim 1 is interpreted by the Examiner as meaning that an activity will not occur, i.e. neuronal cell death will not occur. Undue experimentation would be also required of the skilled artisan to determine the optimal quantity of APC administered, the best route of administration, the duration of treatment, and any possible side-effects to protect all types neuronal cells from cell death. Undue experimentation would also be required of the skilled artisan to "protect" neuronal cells from cell death in subjects having all possible neuropathological disorders.

Furthermore, the specification of the instant application does not teach any methods or working examples that indicate the administration of APC reduces inflammation in a subject having or at risk of having all possible neuropathological disorders. Undue experimentation would be required of the skilled artisan to determine the optimal quantity of APC administered, the location of the target inflammation, the best route of administration, the duration of treatment, and any possible side-effects in order to reduce inflammation in a subject. The specification of the instant application does not teach any methods or working examples to indicate that the administration of APC reduces inflammation in a subject having or at risk of having all possible inflammatory vascular diseases. Undue experimentation would be required of the skilled artisan to determine the optimal quantity of APC administered, the best route of administration, the duration of treatment, and any possible side-effects in order to reduce vascular inflammation in a subject.

Furthermore, a large quantity of experimentation would be required of one skilled in the art to identify a subject population at risk of having all possible neuropathological disorders and inflammatory vascular diseases that require the administration of APC. The specification of the instant application also does not teach any methods or working examples that administer any additional factors or agents in conjunction with APC, other than Protein S. Undue experimentation would be required of the skilled artisan to determine the optimal quantity of all possible neuroprotective agents, anti-thrombotic factors, anti-coagulant agents, and anti-inflammatory agents to be administered to a subject with APC. The skilled artisan would also not be able to predict the effect these various agents would have upon the subject when combined with APC.

Due to the large quantity of experimentation necessary to "protect" neuronal cells from cell death and to reduce inflammation in a subject having or at risk of having a neuropathological disease or inflammatory vascular disease, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of administering all possible neuroprotective agents, anti-thrombotic factors, anti-coagulant agents, or anti-inflammatory agents, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-16 and 19-21 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. The term "neuroprotective amount" in claims 1-8, 16, and 19-21 is a relative term which renders the claim indefinite. The term "neuroprotective amount" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The appropriate dosage range of APC that is required to "protect" neuronal cells from cell death in a subject cannot be determined.

8. The term "anti-inflammatory effective amount" in claims 9-16 and 19-21 is a relative term which renders the claim indefinite. The term "anti-inflammatory effective amount" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The appropriate dosage range of APC that is required to reduce inflammation in a subject cannot be determined.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-2, 9-10, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Griffin et al. (U.S. Patent No. 5,084,274).

Griffin et al. teaches the intravenous administration of activated protein C (APC) to subjects (col 3, lines 8-19; col 5-8).

It is noted to Applicant that a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Taylor, Jr. et al. U.S. Patent 5,009,889

Grinnell et al. U.S. Patent 6,008,199

Grinnell et al. U.S. Patent 6,268,337

Grinnell et al. U.S. Patent 6,426,071

Schwarz et al. U.S. Patent 5,254,532

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

BEB
Art Unit 1647
September 27, 2002

Gary L. Kunz

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